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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/626,315	07/24/2003	Kenneth Il Eckels	Army156A	1691

7590 07/06/2006

U.S. Army Medical Research and Materiel Command
504 Scott St.
Ft. Detrick, MD 21702-5012

EXAMINER	
PARKIN, JEFFREY S	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 07/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/626,315	ECKELS ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 September, 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-6 and 17-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-6 and 17-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *see attached*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Office Action

Status of the Claims

Claims 4-6 and 17-39 are pending in the instant application.

35 U.S.C. § 120

Applicants are reminded that if priority under 35 U.S.C. § 120 based upon a previously filed copending application is desired, specific reference to the earlier filed application should be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. **The status of non-provisional application(s) (whether patented or abandoned) should also be included.** If a parent application has become a patent, the expression "now Patent No._____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application. If applicant desires priority based upon a National Stage filing, this information should also be referenced in the first sentence of the specification (i.e., This application is a National Stage entry of International Application No. PCT/CCPY/NNNNN, filed , 199N). Application No. 10/626,315 is now **PATENT No. 6,638,514.**

37 C.F.R. § 1.98

The information disclosure statements filed 24 July, 2003, 02 June, and 16 September, 2004, have been placed in the application file and the information referred to therein has been considered.

35 U.S.C. § 112, Second Paragraph

Claims 4-6 and 17-39 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Two separate requirements are set forth under this statute: (1) the claims must set forth the subject matter that applicants regard as their invention; and (2) the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant. The claims reference two attenuated dengue viruses (DEN-1 PTA-4810 and DEN-4 PTA-4811) that do not appear in the specification. The only ATCC numbers pertaining to attenuated DEN-1 and DEN-4 viruses were VR-2648 and VR-2652, respectively. Appropriate clarification is required.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Biological Deposit Requirement

Claims 4-6 and 17-39 are rejected under 35 U.S.C. § 112, first paragraph, as failing to provide an enabling disclosure for the claimed invention. It is apparent that the attenuated dengue viruses having the ATCC Nos. PTA-4810, VR-2653, VR-2647, and PTA-4811 are required to practice the claimed invention. Accordingly, as required elements they must be known and readily

available to the public or obtainable by a repeatable method set forth in the specification. However, the specification does not provide a repeatable method for obtaining attenuated viruses with the identical genotypic and phenotypic properties of the deposited strains. First, the specification fails to provide a description of the claimed attenuated viruses and their methods of preparation. Second, it is well-known in the art that the flaviviruses, particularly the dengue viruses, display considerable genotypic and phenotypic heterogeneity (Trent *et al.*, 1989; Rico-Hesse *et al.*, 1998; Holmes and Burch, 2000). Third, it has also been well-documented in the prior art that the repeated passage of RNA viruses in any given cell line leads to unpredictable changes in the genotype of the virus (Harrison *et al.*, 1977; Kinney *et al.*, 1997). Thus, such selection procedures are non-specific and do not yield reproducible changes in the viral genome.

It is noted that the claimed attenuated viruses all display ATCC numbers. However, the disclosure fails to describe said isolates and it is not readily manifest that said isolates were deposited according to the required terms. Applicants are reminded that if a deposit is made under the terms of the Budapest Treaty, then **an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature,** stating that **the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent,** would satisfy the deposit requirements. See 37 C.F.R. § 1.808.

If the deposits have not been made under the provisions of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of the application, access to the deposits will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent;

(c) the deposits will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 C.F.R. § 1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition, the identifying information set forth in 37 C.F.R. § 1.809(d) should be added to the specification. See 37 C.F.R. § 1.803-1.809 for additional explanation of these requirements.

New Matter

Claims 4-6 and 17-39 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the

claimed invention. *In re Rasmussen*, 650 F.2d 1212, 211 U.S.P.Q. 323 (C.C.P.A. 1981). *In re Wertheim*, 541 F.2d 257, 191 U.S.P.Q. 90 (C.C.P.A. 1976). The claims reference two attenuated dengue viruses (DEN-1 PTA-4810 and DEN-4 PTA-4811) that do not appear in the specification. The only ATCC numbers pertaining to attenuated DEN-1 and DEN-4 viruses were VR-2648 and VR-2652, respectively. Thus, applicants do not appear to be in possession of the claimed invention.

Scope of Enablement

Claims 4-6 and 17-27 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not reasonably enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The claims are broadly directed toward methods of inducing a dengue-virus specific immune response in an individual by administering an immunogenic composition comprising various attenuated dengue viruses. The disclosure appears to describe the preparation of four serially passaged attenuated DEN isolates (e.g., DEN-1, DEN-2, DEN-3, and DEN-4) derived from parent DEN vaccine strains. Appropriately drafted claim language directed toward immunogenic compositions comprising specific attenuated dengue viruses, as supported by the disclosure, would be acceptable (i.e., An immunogenic composition comprising more than one attenuated dengue virus selected from the group consisting of an attenuated DEN-1 virus having the ATCC No. VR-2648, an attenuated DEN-2 virus having the ATCC No. VR-2653, ...). However, the claims are not enabled for the full breadth directed toward a method employing any attenuated DEN virus.

The legal considerations that govern enablement determinations pertaining to undue experimentation are disclosed in *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988) and *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

1) The disclosure fails to provide adequate guidance pertaining to the molecular determinants responsible for the attenuated phenotype of any given virus. In order to reproducibly generate a virus with the desired phenotype, the skilled artisan would require a knowledge of the molecular determinants modulating the phenotypic properties of the virus. However, the disclosure fails to identify those regions of the dengue virus genome that can be manipulated in such a manner as to produce the desired effect. Molecular characterization studies of the various attenuated DEN isolates discussed in the specification were not performed. Thus, the basis for the attenuated phenotype of any given dengue strain remains to be elucidated.

2) The disclosure fails to provide a reproducible method for generating attenuated viruses with the same genotypic and phenotypic properties. The specification relies upon a serial passage technique for the generation of an attenuated virus. However, it has been well-documented that serial passage

techniques do not provide a reproducible and reliable means for generating viruses with the same genotypic and phenotypic properties (Harrison *et al.*, 1977; Kinney *et al.*, 1997). Thus, the skilled artisan cannot readily predict the genotype or phenotype of any given virus produced by these techniques.

3) The dengue viruses display considerable genotypic and phenotypic heterogeneity thereby complicating their use as a vaccine or immunogenic composition (Trent *et al.*, 1989; Rico-Hesse *et al.*, 1998; Holmes and Burch, 2000). Because these viruses exist as a quasispecies, it is difficult to predict which genotypic changes will produce an attenuated virus with the desired phenotype.

4) The disclosure fails to provide a sufficient number of working embodiments. It appears that a small and limited number of attenuated viruses were generated or obtained. However, these viruses were not characterized at the molecular level and other attenuated DEN isolates were not described.

5) The claims are of excessive breadth and encompass any and all attenuated dengue viruses. However, as noted above, the disclosure fails to provide sufficient support for such claim breadth because appropriate guidance pertaining to the genotypic and phenotypic characteristics of said viruses is not provided.

The first paragraph of § 112 requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification. *In re Fisher*, 427 F.2d 833, 839, 166 U.S.P.Q. 18, 24 (C.C.P.A. 1970). *In re Vaeck*, 20 U.S.P.Q.2d 1438 (C.A.F.C. 1991). *In re Angstadt*, 537 F.2d 498, 502-03, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976). The court stated in *In re Vaeck* that "It is well settled that patent applicants are not required to disclose every species encompassed by their claims, even in an unpredictable art. *In re*

Angstadt, 537 F.2d 498, 502-03, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976). However, there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and how to use the invention as broadly as it is claimed. This means that the disclosure must adequately guide the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility. Where, as here, a claimed genus represents a diverse and relatively poorly understood group of microorganisms, the required level of disclosure will be greater than, for example, the disclosure of an invention involving a "predictable" factor such as a mechanical or electrical element." Thus, when all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation from the skilled artisan to practice the claimed invention.

35 U.S.C. § 103(a)

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 4-6 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the combined teachings of Edelman *et al.* (1994), Vaughn *et al.* (1996), Angsbhakorn *et al.* (1994), and Hoke *et al.* (1990). The references disclose methods for stimulating dengue-virus specific immune responses by administering immunogenic compositions comprising attenuated DEN-1, DEN-2, DEN-3, or DEN-4 viruses, respectively. These teachings do not disclose a method that employs a multivalent dengue virus immunogenic composition. However, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine all four attenuated dengue viruses in various combinations to prepare multivalent immunological reagents and to utilize said reagents in a method to induce antisera that are capable of recognizing multiple DEN isolates. Such reagents would facilitate further immunological and biochemical studies involving the dengue viruses.

Statutory Type Double Patenting, 35 U.S.C. § 101

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. § 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. *Miller v. Eagle Mfg. Co.*, 151 U.S.P.Q. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 U.S.P.Q. 330 (C.C.P.A. 1957); and *In re Vogel*, 422 F.2d 438, 164 U.S.P.Q. 619 (C.C.P.A. 1970). A statutory type (35 U.S.C. § 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer **cannot** overcome a double patenting rejection based upon 35 U.S.C. § 101.

Claims 28-39 are rejected under 35 U.S.C. § 101 as claiming the same invention as that of claims 1-12 of prior U.S. Patent No. 6,638,514. This is a double patenting rejection.

Correspondence

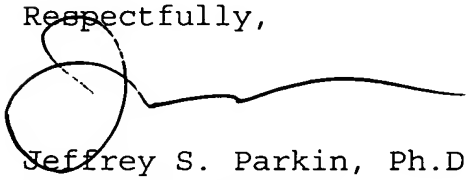
Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Bruce R. Campell, Ph.D., can be reached at (571) 272-0974. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Applicants are reminded that the United States Patent and Trademark Office (Office) requires most patent related correspondence to be: a) faxed to the Central FAX number (571-

273-8300) (updated as of July 15, 2005), b) hand carried or delivered to the Customer Service Window (now located at the Randolph Building, 401 Dulany Street, Alexandria, VA 22314), c) mailed to the mailing address set forth in 37 C.F.R. § 1.1 (e.g., P.O. Box 1450, Alexandria, VA 22313-1450), or d) transmitted to the Office using the Office's Electronic Filing System. This notice replaces all prior Office notices specifying a specific fax number or hand carry address for certain patent related correspondence. For further information refer to the Updated Notice of Centralized Delivery and Facsimile Transmission Policy for Patent Related Correspondence, and Exceptions Thereto, 1292 Off. Gaz. Pat. Office 186 (March 29, 2005).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,



Jeffrey S. Parkin, Ph.D.
Primary Examiner
Art Unit 1648

26 June, 2006